

Contents lists available at [ScienceDirect](http://www.sciencedirect.com)

Respiratory Medicine Case Reports

journal homepage: www.elsevier.com/locate/rmcr

Case report

A severe H7N9 pneumonia with syndrome of inappropriate antidiuresis and vitamin D deficiency[☆]Leng Lin^a, Jin Yao^a, Gang Chen^b, Caijing Lin^{c,*}^a Department of Infectious Disease, Fujian Provincial Hospital, Fujian Medical University, Fuzhou 350001, China^b Department of Endocrinology, Fujian Provincial Hospital Key Laboratory of Endocrinology, Fujian Medical University, Fuzhou 350001, China^c Department of Emergency, Fujian Provincial Hospital, Fujian Medical University, Fuzhou 350001, China

A B S T R A C T

Keywords:

H7N9 pneumonia

Syndrome of inappropriate antidiuresis

Vitamin D deficiency

Objective: Some H7N9 patients presented with hyponatremia. But whether SIAD could be the etiology of hyponatremia in H7N9 pneumonia is still not known.**Design, setting, and participants:** A H7N9 patient was enrolled. Clinical sign were evaluated. Effective osmolality, urinary osmolality, urinary sodium, thyroid function, adrenal function, 25(OH) Vitamin D and cellular immune function were measured.**Results:** (1) The results showed low serum osmolality, inappropriately elevated urine osmolality, elevated urine sodium concentration, low serum uric acid concentration, relatively normal serum creatinine concentration, normal acid-base and potassium balance, normal adrenal and thyroid function in our patient. (2) Our patient showed vitamin D deficiency and decline of cellular immune function.**Conclusions:** Some H7N9 pneumonia could cause SIAD. Early detection and appropriate treatment of SIAD in H7N9 pneumonia might be important. Our patient showed vitamin D deficiency and decline of cellular immune function.© 2014 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/3.0/>).

The first identified cases of human infection with a novel influenza A (H7N9) virus occurred in eastern China during February and March 2013 and were characterized by rapidly progressive pneumonia, respiratory failure, acute respiratory distress syndrome (ARDS), and fatal outcomes. Here we report a severe H7N9 pneumonia with syndrome of inappropriate antidiuresis and vitamin D deficiency.

A 68-year-old male patient was admitted because of cough, fever and dyspnea for 1 day. He reported a history of contact with poultry. He had been well expect coronary disease and chronic obstructive pulmonary disease (COPD) before admission. He denied using steroid before. On examination, the temperature was 39.7 °C, pulse was 78 beats/min, respiratory rate was 30 breaths/min, and blood pressure was 112/78 mmHg. The patient was alert and oriented and appeared fatigued. The patient had a sickly appearance, shortness of breath, cyanotic lipst. Moist rales were present in both lungs. The abdomen was soft and nontender, with normal bowel sounds. No edema was found in the lower limbs. The rest of the

examination was reportedly normal. The white cell count revealed WBC of $2.7 \times 10^9/L$, N% of 67%, L% of 23%. The blood levels of electrolytes revealed hyponatremia (125 mmol/L), hypophosphatemia (0.55 mmol/L), normal serum potassium (4.4 mmol/L) and calcium (2.27 mmol/L). Patient showed vitamin D deficiency (13.9 ng/ml). The results of renal-function tests showed hypouricemia (106 mmol/L) and the rest were normal. Blood glucose and triglyceride were normal. Serum osmolality is 263 mOsm/kg. Urine osmolality is 570 mOsm/kg. Urine sodium concentration was 89 mmol/L. ACTH and cortisol at 8am were normal (ACTH 22.2 pg/ml, Cor 488 nmol/L). Thyroid function was normal. CD4+ T-cell count were 120/UI (normal range 410–1590/UI) and CD4+/CD8+ were 0.81, which suggested decline of cellular immune function. C-reactive protein (CRP) was 82.1 mg/L (0–3 mg/L), ESR was 22 mm/h (0–15 mm/h), Procalcitonin was 0.26 ng/ml (<0.05 ng/ml); D dimmer was 2.58 µg/ml (0.0–0.5 µg/ml). Blood gas analysis (FiO₂ = 29%) indicated PH 7.47, PCO₂ 27 mmHg, PO₂ 63 mmHg. Chest CT revealed inflammation of both lungs especially in the right lung (Fig. 1). Real time RT-PCR by CDC confirmed H7N9 infection. The patients were diagnosed H7N9 pneumonia with syndrome of inappropriate antidiuresis and vitamin D deficiency [1]. The patient began appropriate fluid restriction and salt administration. The patient was treated with oseltamivir to fight

[☆] This study was proved by IRB of Fujian Provincial Hospital and written informed consent was obtained from the patient.

* Corresponding author.

E-mail address: caijinglin_fq@163.com (C. Lin).

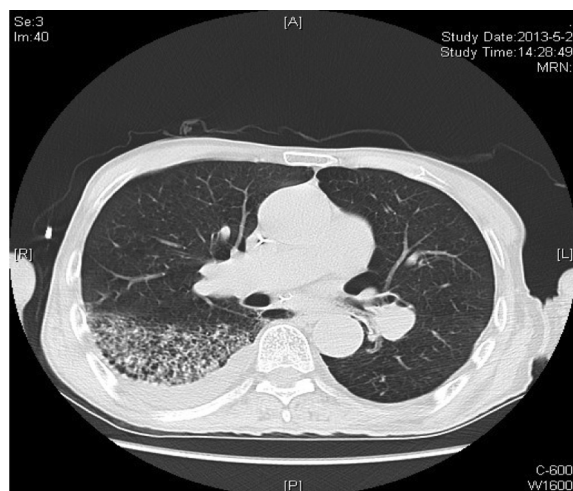


Fig. 1. Chest CT of case.

the virus and cefoperazone to fight infection. The patient was also administered methylprednisolone 40 mg/d for 3 days. Non-invasive mechanical ventilation, thymalfasin, rocalirol and supportive treatment were provided as well. The patient was discharged from hospital after three weeks.

Discussion

Here we reported a severe H7N9 pneumonia with syndrome of inappropriate antidiuresis (SIAD) and vitamin D deficiency.

From the above we knew our patient had hyponatremia. Hyponatremia was the most common electrolyte abnormality in hospitalized patients occurring in up to 11% of elderly patients in hospital [1]. Hyponatremia was important to recognize both because of potential morbidity and because it can be a marker of underlying disease. SIAD was the most frequent cause of hyponatremia, although hyponatremia associated with volume depletion of the extracellular fluid also occurs commonly [2]. Although the causes of SIAD were myriad, they could be categorized as related to malignant diseases, pulmonary diseases, and disorders of the central nervous system, among others. Our patient had low serum osmolality, inappropriately elevated urine osmolality (above 300 mOsm/kg), urine sodium concentration above 40 mmol/L, low serum uric acid concentration, relatively normal serum creatinine concentration, normal acid–base and potassium balance, normal adrenal and thyroid function. The patients could be diagnosed SIAD according the diagnostic criteria of SIAD [3]. An association between hyposmolality and pulmonary disease had been known for over 50 years. In 1937, Winkler and Crankshaw were the first to focus attention on hyponatremia seen in patients with pulmonary tuberculosis and bronchogenic carcinoma who had normal adrenal function [4]. Pulmonary infections were a well-documented cause of hyposmolality and hyponatremia [5]. In this study we reported a novel H7N9 virus pneumonia could also cause SIAD. The mechanism(s) whereby pulmonary infections lead to SIAD was not entirely known. Dreyfuss and associates's study suggested that pneumonia may increase plasma vasopressin levels by altering the osmoregulation of central vasopressin release such that a lower plasma osmolality is required to fully suppress vasopressin release [6]. This was known as the “reset osmostat” hypothesis. An important clinical question was whether SIAD or hyponatremia could influence prognosis of pneumonia. Some studies suggested

that both SIAD and hyponatremia had negative impact in elderly patients with pneumonia. Miyashita and colleagues reported that mortality in elderly patients with aspiration pneumonia was significantly associated with SIAD [7]. A study by Nair and colleagues reported some increased risk of death with hyponatremia [8]. Many important clinical issues were raised from our case report. First, whether SIAD or hyponatremia was associated with adverse outcome in H7N9 pneumonia? Second, whether SIAD or hyponatremia correction would improve prognosis of H7N9 pneumonia. Above mentioned studies suggested that mortality in elderly patients with pneumonia might be significantly associated with SIAD or hyponatremia [7,8]. If it was the case, aggressive treatment of H7N9 pneumonia to correct inappropriate antidiuresis and appropriate treatment of hyponatremia were all important therapeutic measurements to reduce mortality of severe H7N9 pneumonia.

Our patient also showed vitamin D deficiency and cellular immune dysfunction, which suggested that vitamin D deficiency might be one of the factors which resulted in decreased cellular immune function. Since vitamin D was known to possess anti-inflammatory and immune-modulating effects, whether vitamin D deficiency population were susceptible to H7N9 pneumonia [9,10]? Whether vitamin D deficiency before H7N9 pneumonia would lead to adverse outcome in H7N9 infection and whether vitamin D replacement therapy will improve the outcome of H7N9 pneumonia? All of the above questions were still unknown. Prospective studies should be conducted to answer aforementioned questions. In our opinion, vitamin D should be measured in severe H7N9 pneumonia. We used rocalirol to correct vitamin D deficiency in our patient.

In conclusion, our case report suggested that SIAD should be suspected in H7N9 patients with hyponatremia, hyposmolality, and a urine osmolality above 100 mOsm/kg. Vitamin D deficiency could be associated with decreased cellular immune function in severe H7N9 pneumonia. Prospective or retrospectively studies should be conducted to confirm our hypothesis.

Funding

China's National Natural Science Fund (81270874).

References

- [1] Sunderam SG, Mankikar GD. Hyponatraemia in the elderly. *Age Ageing* 1983;12:77–80.
- [2] Berghmans T, Paesmans M, Body JJ. A prospective study on hyponatraemia in medical cancer patients: epidemiology, aetiology and differential diagnosis. *Support Care Cancer* 2000;8:192–7.
- [3] Ellison DH, Berl T. The syndrome of inappropriate antidiuresis. *N Engl J Med* 2007;356:2064–72.
- [4] Winkler AW, Crankshaw OF. Chloride depletion in conditions other than Addison's disease. *J Clin Invest* 1938;17:1–10.
- [5] Rose CE, Dixon BS, Anderson RJ. Water metabolism in respiratory disorders. *Semin Nephrol* 1984;4:295–302.
- [6] Dreyfuss D, Levie F, Paillard M, Rahmani J, Coste F. Acute infectious pneumonia is accompanied by a latent vasopressin-dependent impairment of renal water excretion. *Am Rev Respir Dis* 1988;138:583–9.
- [7] Miyashita J, Shimada T, Hunter AJ, Kamiya T. Impact of hyponatremia and the syndrome of inappropriate antidiuresis on mortality in elderly patients with aspiration pneumonia. *J Hosp Med* 2012;7:464–9.
- [8] Nair V, Niederman MS, Masani N, Fishbane S. Hyponatremia in community-acquired pneumonia. *Am J Nephrol* 2007;27:184–90.
- [9] Aregbesola A, Voutilainen S, Nurmi T, Virtanen JK, Ronkainen K, Tuomainen TP. Serum 25-hydroxyvitamin D3 and the risk of pneumonia in an ageing general population. *J Epidemiol Community Health* 2013;67:533–6.
- [10] Venkatram S, Chilimuri S, Adrish M, Salako A, Patel M, Diaz-Fuentes G. Vitamin D deficiency is associated with mortality in the medical intensive care unit. *Crit Care* 2011;15:R292.